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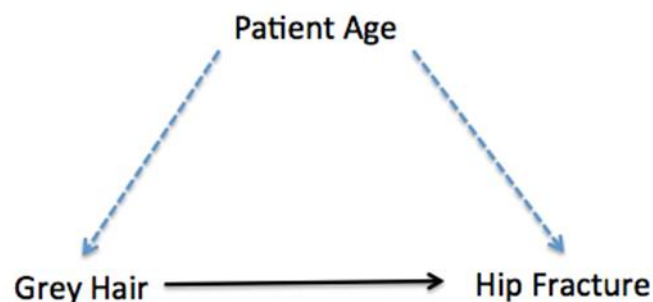
Efficacy versus effectiveness in clinical trials

Costa ML⁽¹⁾, Griffin XL⁽¹⁾, Parsons NR⁽²⁾, Dritsaki M⁽¹⁾ and Perry DC⁽¹⁾,

Correspondence to M. Costa; email: matthew.costa@ndorms.ox.ac.uk

The Bone & Joint Journal is keen on randomised clinical trials. The reason for this is straightforward. Randomisation is a simple and highly effective way of reducing the effects of ‘confounding factors’ in comparative research. Trauma and orthopaedic surgery has some of the most effective interventions in medicine. However, all surgical interventions are ‘complex’ in that they have many interacting facets which each contribute to the overall result. The selection of patients, the preoperative pathway, the anaesthetic technique, the experience of the surgeon, the nursing and therapy staff, and even the hospital food, can all have an influence on the outcome. Any factor that is independently related to both the intervention and the outcome is called a ‘confounder’ (Fig. 1). Whilst some confounding variables can be identified and measured, such as the age of the patients, others may be unknown or difficult to measure, such as the influence of surgical expertise. Therefore, confounding is always a problem in trauma and orthopaedic research, even if we are able to match the patients taking part in a trial carefully.

Figure 1. Researchers identify a strong association between grey hair and hip fracture. Patient age is independently associated with both grey hair colour, and hip fracture. Patient age is therefore a confounding variable.



We have previously provided guidance on aspects of reporting randomised trials in The Bone & Joint Journal,¹⁻³ and the overall quality of reporting is improving all the time. A new requirement of prospective registration of the details of trials will, hopefully, push us further in the right direction.⁴ However, there is still plenty of room for confusion. One common area of difficulty is the reporting of ‘efficacy’ versus ‘effectiveness’ randomised trials.

What does this mean and why is the distinction important?

Efficacy trials report the results of tightly defined interventions, provided to highly selected participants in optimal surroundings. They usually involve a single centre and, because of the highly controlled design, usually have smaller sample sizes. Such designs are often described as ‘experimental’. Efficacy trials provide estimates of the ‘best possible’ effect of an intervention. A good example is the recent trial from van der Woude et al.⁵ This exciting trial may represent a major step forward in the management and surgical approach to a common orthopaedic problem if, and only if, the results can be reproduced more broadly.

Effectiveness trials seek to establish the effect of different interventions when they are delivered in the context of a whole healthcare system. In such studies the eligibility criteria

are usually broader and the interventions take place in less controlled environments; thus, in any institution where the intervention may be delivered, by any team who are able to do so. Many surgeons, anaesthetists and therapists are typically involved in such trials, and they are usually multi-centre and involve many more patients. Effectiveness trials are designed to reflect how the intervention works in the real world context of the healthcare system in which it is tested. These designs are often termed ‘pragmatic’. A recent example is the Distal Radius Acute Fracture Fixation Trial,^{6,7} which investigated the use of locking plates compared with K-wires for the fixation of dorsally displaced fractures of the distal radius. Almost any adult patient with this fracture was eligible and over 200 surgeons took part in 18 centres of varying size and specialism. The trial was designed to replicate current practice across the NHS in the United Kingdom, and has subsequently been used to shape both practice and policy.^{8,9}

It is important to stress that neither type of design is correct or incorrect; both have a role in the research ‘pathway’. Efficacy (experimental) designs are often used early on in the implementation of a new intervention. Investigators seek to control as much of the design of the study as possible to provide evidence towards the best possible outcomes for the new intervention. These studies have the potential to change clinical practice, but can the results described in these experimental trials be reproduced in the real world? Effectiveness (pragmatic) trials are then warranted. Unfortunately, there are many examples where promising results described in the experimental setting do not translate well into the broader health service environment.¹⁰

In reality, the difference between the design of an experimental and a pragmatic trial is not black and white. Pragmatism is a spectrum ranging from the first report of a new device by the design-surgeon in one centre with specific participants, through to the large, multicentre trials favoured by the makers of guidelines and policies. An understanding of the distinction between the designs of trials is particularly important for readers, in order to consider how best to apply the research findings.

Guidance for potential authors

If you are reporting an efficacy trial with an experimental design, tell us upfront. Describe your eligibility criteria in detail, tell us about the experience and involvement of the surgeon/centre providing the intervention and explain why you are using detailed, potentially complicated outcome tools. The reader will then understand the context of the trial and will be able to judge whether or not they can replicate these interventions in their own practice. It is always helpful if you report the limitations inherent in efficacy trials in the discussion section of your paper. Can these results be replicated elsewhere? Similarly, if you are reporting an effectiveness trial, and use the word pragmatic at the beginning of your report, the reader will know to expect broad eligibility criteria, many centres and surgeons and patient-focused outcome measures. The limitations section of the paper should then invariably reflect on how pragmatic the trial is. Does this trial really replicate clinical practice in your healthcare setting?

We are, of course, delighted to receive both types of trial design at The Bone & Joint Journal.

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Affiliations:

- (1) University of Oxford,
NDORMS, Oxford Trauma,
Kadoorie Centre, John Radcliffe
Hospital, Oxford, OX3 7UD, UK.
- (2) University of Warwick,
Statistics and Epidemiology,
Warwick Medical School,
Coventry CV4 7AL, UK.
- (3) University of Liverpool,
Institute of Translational
Medicine, Easton Rd, Liverpool
L12 2AP, UK.